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154673 RECEIVED

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SEARCH REQUEST FORM

MAY 27 2005

Scientific and Technical Information Center

(STIC)

Requester's Full Name: Molly Ceperley Examiner #: 59757 Date: 05/27/05

Art Unit: 1641 Phone Number ~~30~~ 2-0813 Serial Number: PCT/US04/38640

Mail Box and Bldg/Room Location: ~~Rem 3A51~~ → Rem 3C70 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

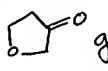
Title of Invention: See bibliographic data sheet attached.

Inventors (please provide full names):

Earliest Priority Filing Date: 11/21/03

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search for the compounds of claims 1, 3 and 6. These are FK506 (tacrolimus) derivatives which bind immunophilins.

Note that C24 is substituted with -O-C(=O)-NH-m and is NOT part of a  group.

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable
Searcher:	NA Sequence (#)		STN
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Date Searcher Picked Up:	Bibliographic		Dr.Link
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Searcher Prep & Review Time:	Fulltext		Sequence Systems
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Online Time:	Other		Other (specify)

PTO-1590 (8-01)

10/719,868

Ceperley ~~10/394,108~~ wrong number 06/02/2005

Considered WEC 07/22/05

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STRUCTURE FILE UPDATES:     1 JUN 2005  HIGHEST RN 851509-21-2
DICTIONARY FILE UPDATES:    1 JUN 2005  HIGHEST RN 851509-21-2

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
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http://www.cas.org/ONLINE/DBSS/registryss.html

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FILE COVERS 1907 - 2 Jun 2005  VOL 142 ISS 23
FILE LAST UPDATED: 1 Jun 2005  (20050601/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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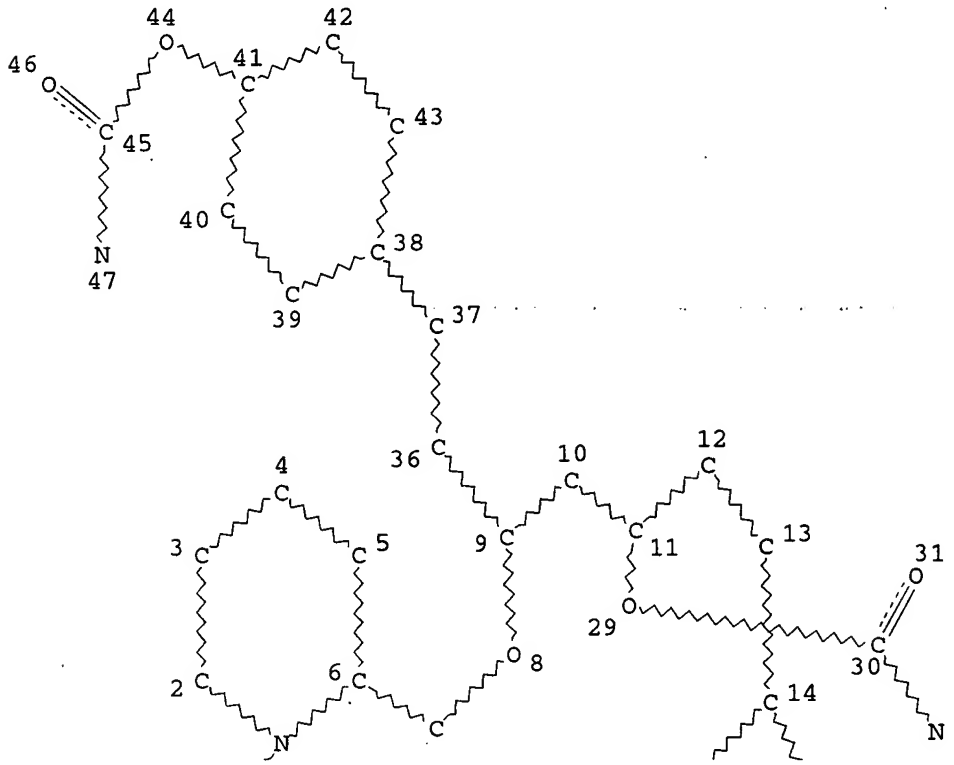

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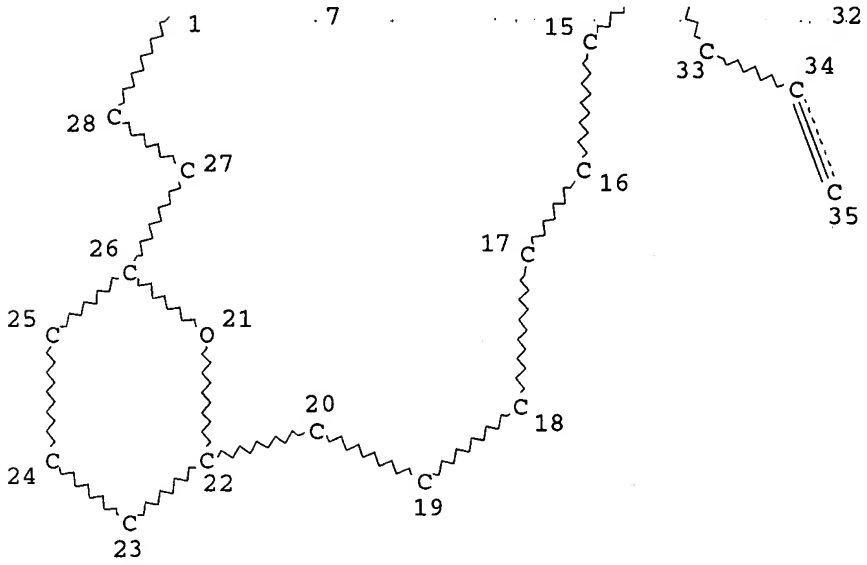

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NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE

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L18 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L17

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L18 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:298362 HCAPLUS
DOCUMENT NUMBER: 120:298362
TITLE: Water-soluble macrocyclic lactones as immunosuppressants and their preparation
INVENTOR(S): Harada, Setsuo; Tanida, Seiichi; Funahashi, Yasunori
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05294973	A2	19931109	JP 1991-162806	19910703
JP 3138872	B2	20010226		

PRIORITY APPLN. INFO.: JP 1990-179760 A1 19900706
OTHER SOURCE(S): MARPAT 120:298362
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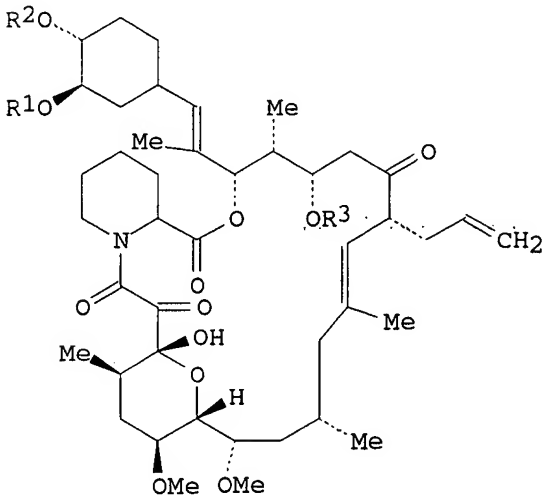

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AB The title compds. I (≥1 of R1-R3 is basic group-containing carbamoyl and the rest is H or protective group) and their salts, useful as immunosuppressants, are prepared by treating I (≥1 of R1-R3 is activated ester and the rest is H or protective group) with basic group-containing amines and optional deprotection of the OH group(s). A solution of 3.20 g FK 506 in CH2Cl2 was treated with ClCO2CHClMe and pyridine at 0° to give 4.03 g I (R1 = Me, R2 = R3 = CO2CHClMe), 1.27 g of which

was stirred with 0.67 mL ethylenediamine in CH2Cl2 at 0° for 3.5 h to give, after treatment with 0.1 N HCl and 8% isobutanol-H2O, 1.10 g I.2HCl (R1 = Me, R2 = R3 = CONHCH2CH2NH2), which showed physiol. saline solubility 15.4 mg/mL and inhibited ConA-induced blastogenesis of spleen cells at IC50 of 41.8 ng/mL.

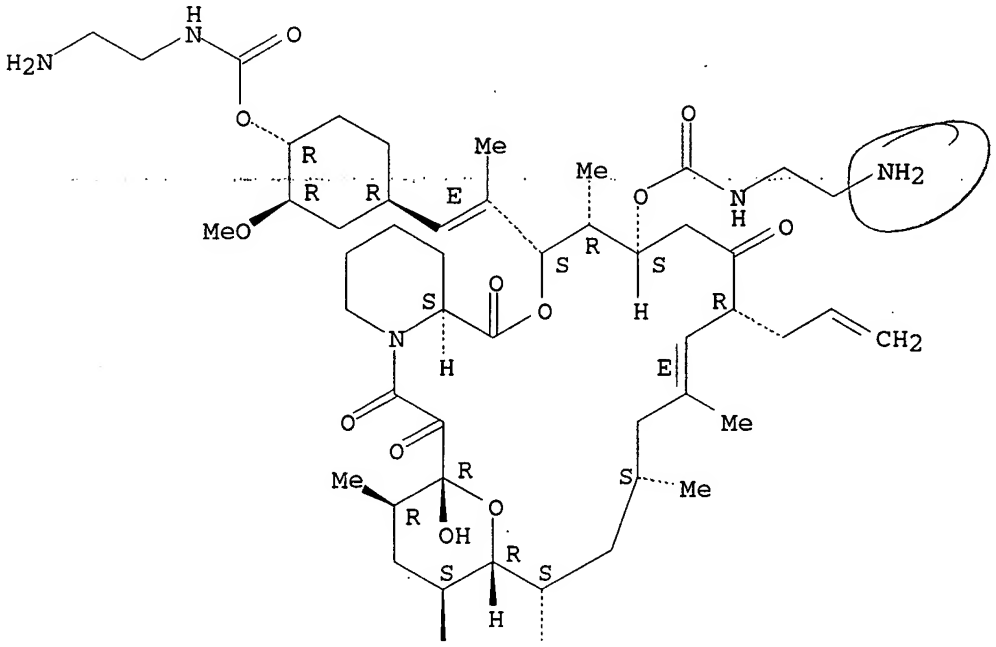
IT **154591-73-8P 154634-68-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, water-soluble, as immunosuppressant)

RN 154591-73-8 HCAPLUS

CN Carbamic acid, (2-aminoethyl)-, 4-[2-[5-[[[(2-aminoethyl)amino]carbonyl]oxy]-1,4,5,6,7,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-19-hydroxy-14,16-dimethoxy-4,10,12,18-tetramethyl-1,7,20,21-tetraoxo-8-(2-propenyl)-15,19-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosin-3-yl]-1-propenyl]-2-methoxycyclohexyl ester, [3S-[3R*[E(1S*,2S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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RN 154634-68-1 HCAPLUS

CN Carbamic acid, (2-aminoethyl)-, 4-[2-[5-[[[(2-aminoethyl)amino]carbonyl]oxy]-1,4,5,6,7,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-19-hydroxy-14,16-dimethoxy-4,10,12,18-

tetramethyl-1,7,20,21-tetraoxo-8-(2-propenyl)-15,19-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosin-3-yl]-1-propenyl]-2-methoxycyclohexyl ester, dihydrochloride, [3S-[3R*[E(1S*,2S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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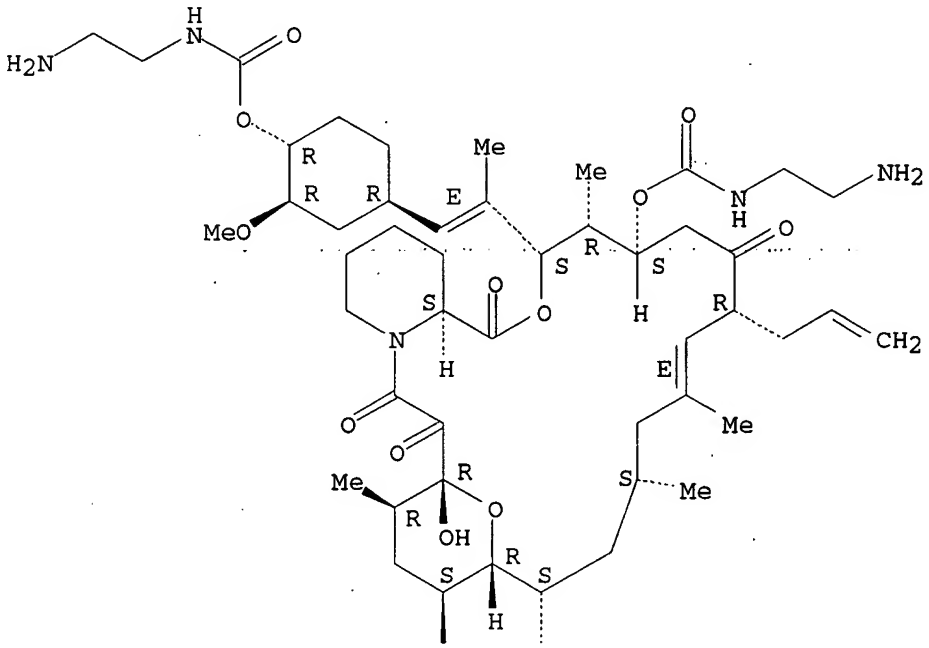

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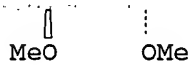

●2 HCl

L18 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:194038 HCAPLUS
DOCUMENT NUMBER: 116:194038
TITLE: Preparation of tricyclic macrocycles as immunosuppressants and antimicrobials
INVENTOR(S): Kasahara, Chiyoshi; Ohkawa, Takehiko; Hashimoto, Masashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9113899	A1	19910919	WO 1991-JP314		19910308
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
JP 05504956	T2	19930729	JP 1991-505321		19910308
PRIORITY APPLN. INFO.:			GB 1990-5521	A	19900312
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OTHER SOURCE(S): MARPAT 116:194038
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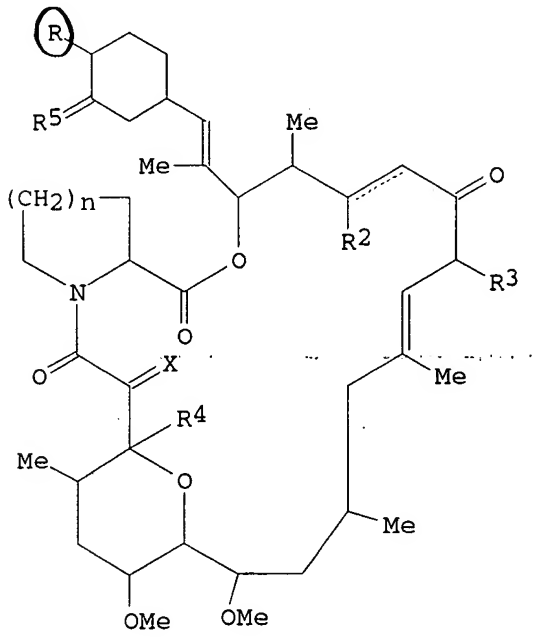

I

AB The title compds. I ([R] = R1NHCO2; [R1] = H, (substituted) C1-6 alkyl, (substituted) aryl; R2 = H, (protected) hydroxy; R3 = Me, Et, Pr, allyl; R4 = OH, alkoxy; R5 = O, (H, OH), (H, alkoxy); X = O, (H, OH); n = 1, 2; dotted line is optional double bond] were prepared as immunosuppressants and antimicrobials. Thus I (R = OH; R2 = H; R3 = allyl; R4 = OH; R5 = (MeO, H); X = O; n = 2; double bond in 14-position and pyridine were dissolved in anhydrous CH2Cl2 and treated with PhN:C:O to give title compound I (R = PhNHCO2, all other defined as above for reactant). A different I (R = 4-ClC6H4NHCO2; optional double bond at 14-position absent; all others defined as above) had IC50 of 1.4 + 10-8 M against in vitro mixed lymphocyte reaction.

IT **137959-62-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunosuppressant and antimicrobial)

RN 137959-62-7 HCAPLUS

CN Carbamic acid, (3-hydroxypropyl)-, 4-[2-[1,4,5,6,7,8,11,12,13,14,15,16,17,

18,19,20,21,23,24,25,26,26a-docosahydro-19-hydroxy-5-[[[(3-hydroxypropyl)amino]carbonyl]oxy]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,7,20,21-tetraoxo-8-(2-propenyl)-15,19-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosin-3-yl]-1-propenyl]-2-methoxycyclohexyl ester (9CI) (CA INDEX NAME)

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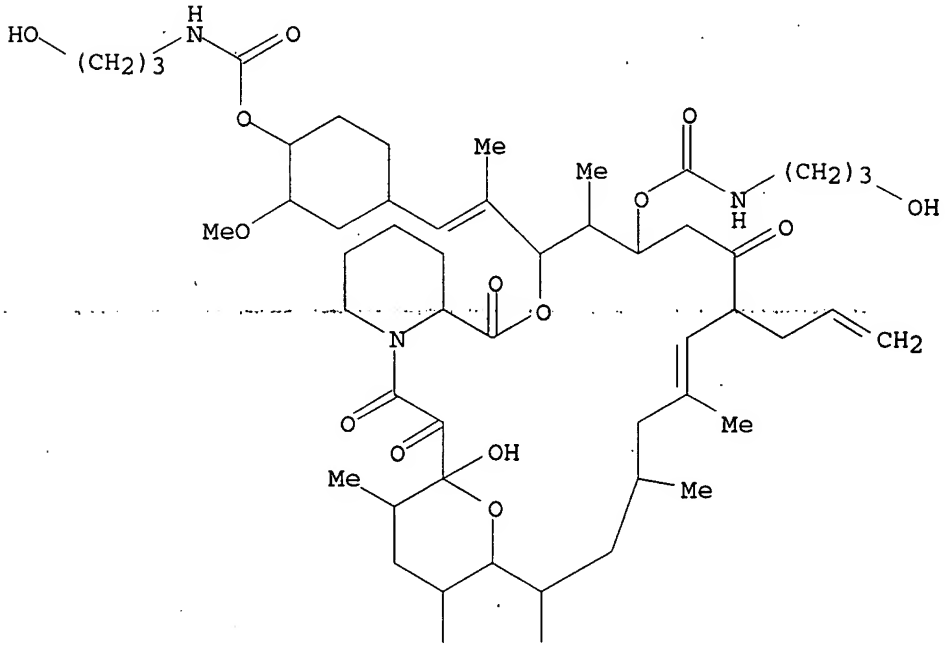

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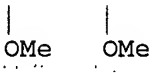

L18 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1991:582958 HCAPLUS
DOCUMENT NUMBER:	115:182958
TITLE:	Preparation of macrocyclic compounds as immunosuppressants
INVENTOR(S):	Donald, David Keith; Hardern, David Norman; Cooper, Martin Edward; Furber, Mark; Hashimoto, Masashi; Kasahara, Chiyoshi; Ohkawa, Takehiko
PATENT ASSIGNEE(S):	Fisons PLC, UK; Fujisawa Pharmaceutical Co., Ltd.
SOURCE:	PCT Int. Appl., 42 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9102736	A1	19910307	WO 1990-GB1262		19900810
W: AU, CA, FI, HU, JP, KR, NO, SU, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
AU 9062866	A1	19910403	AU 1990-62866		19900810
EP 487593	A1	19920603	EP 1990-912790		19900810
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
JP 05504944	T2	19930729	JP 1990-512176		19900810
ZA 9006509	A	19910424	ZA 1990-6509		19900816
CN 1049503	A	19910227	CN 1990-107149		19900818
PRIORITY APPLN. INFO.:			GB 1989-18927	A	19890818
			GB 1989-22653	A	19891009
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OTHER SOURCE(S): MARPAT 115:182958

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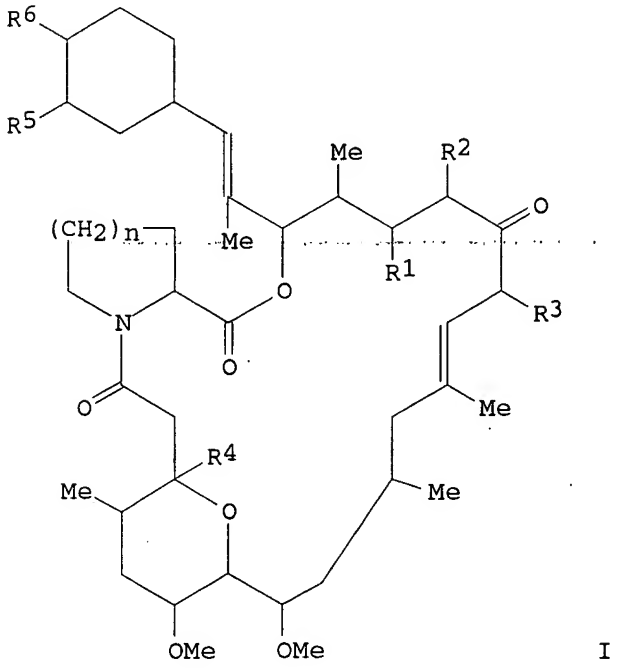

I

AB The title compds. I (R1 = H, OH, alkoxy, R7CO2; R2 = H; or R1R2 = bond; R3 = Me, Et, Pr, etc.; R4 = OH, alkoxy; R5 = OH, MeO; R6 = OH, alkoxy, R8CO2; R7, R8 = alkyl, aryl, NH2, etc.; n = 1 or 2; a proviso is given) were prepared Treatment of 14-acetoxy-12-[2-(4-acetoxy-3-methoxycyclohexyl)-1-methylvinyl]-17-allyl-23,25-dimethoxy-13,19,21,27-tetramethyl-1,2-thioxomethylenedioxy-11,28-dioxa-4-azatricyclo[22.3.1.04,9]octacos-18-ene-3,10,16-trione with tributyltin hydride in refluxing toluene containing AIBN gave a product which was treated with aqueous HCl to give I (R1 = R6 = AcO, R2 = H, R3 = allyl, R4 = OH, R5 = MeO, n = 2) which in vitro exhibited IC50 of 2.4 + 10-8 M against the mixed lymphocyte reaction.

IT **134695-39-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as immunosuppressant)

RN 134695-39-9 HCAPLUS

CN Carbamic acid, (4-chlorophenyl)-, 4-[2-[5-[[[(4-chlorophenyl)amino]carbonyl]oxy]-1,4,5,6,7,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-19-hydroxy-14,16-dimethoxy-4,10,12,18-tetramethyl-1,7,21-trioxo-8-(2-propenyl)-15,19-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosin-3-yl]-1-propenyl]-2-methoxycyclohexyl ester (9CI) (CA INDEX NAME)

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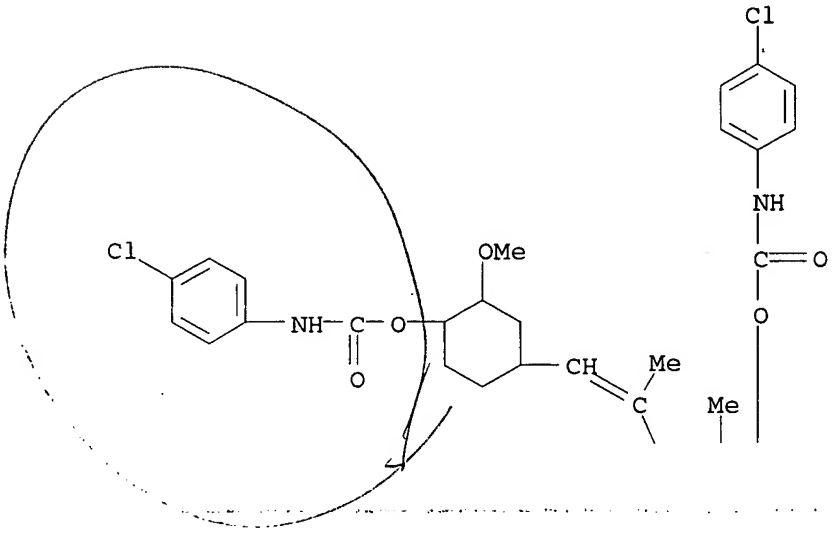

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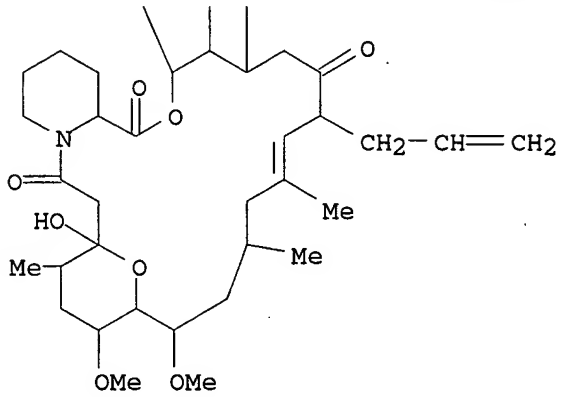

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FILE CONTENT: 1988-PRESENT (VOL 142 ISS 22)(20050527/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US    6864386 08 MAR 2005
DE   10337309 10 MAR 2005
EP    1518545 30 MAR 2005
JP 2005060524 10 MAR 2005
WO 2005037841 28 APR 2005

Structure search limits have been raised.  See HELP SLIMIT for the new,
higher limits.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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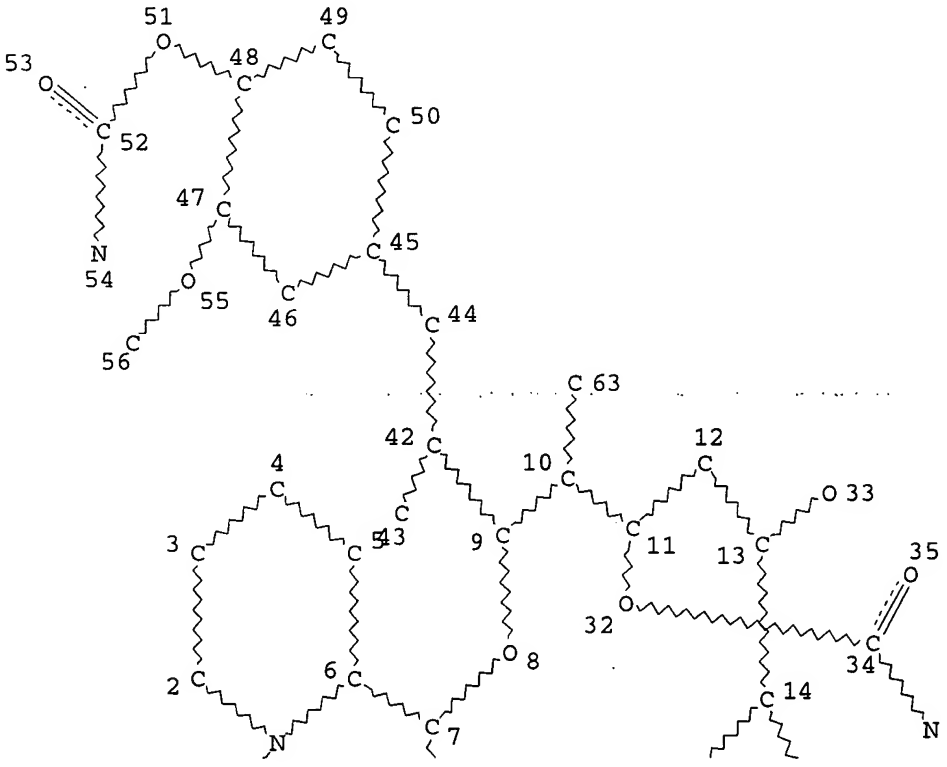

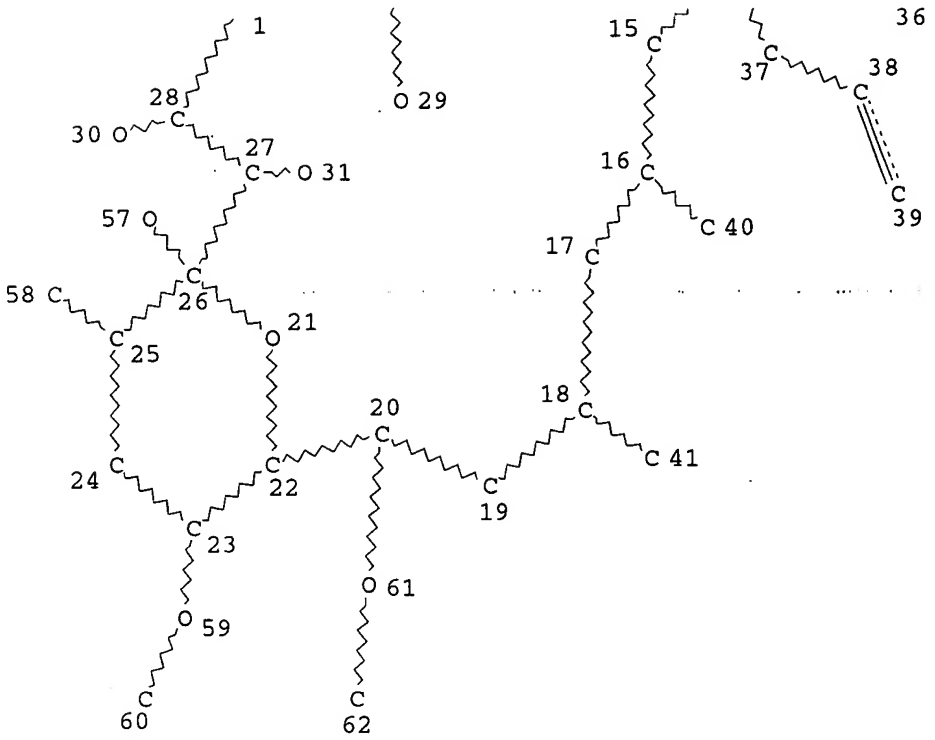

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STEREO ATTRIBUTES: NONE
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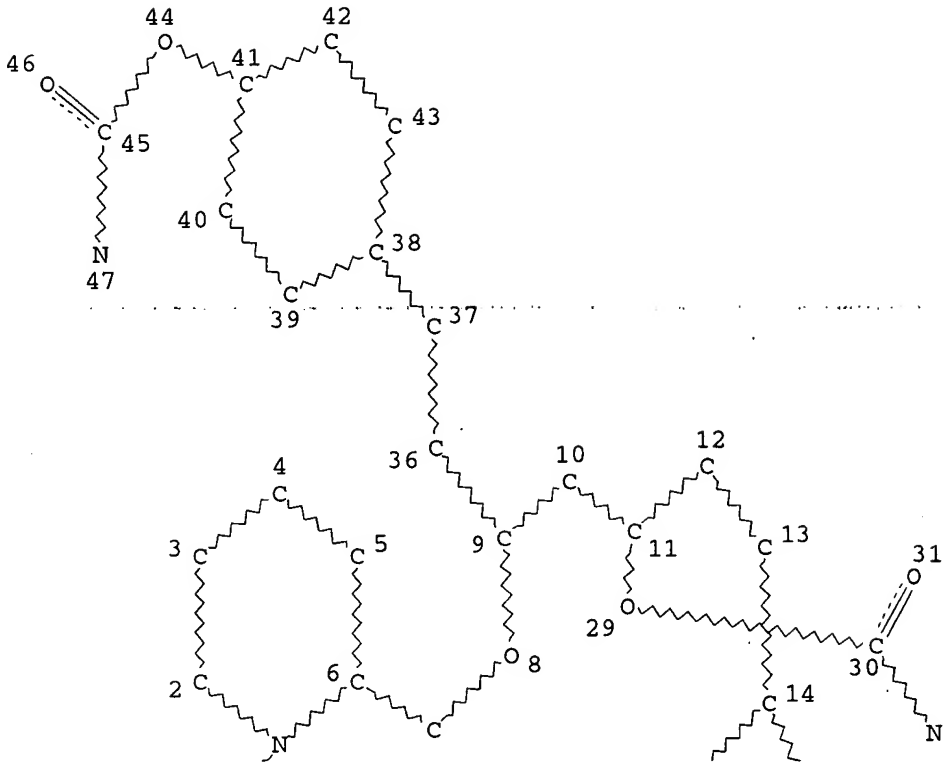

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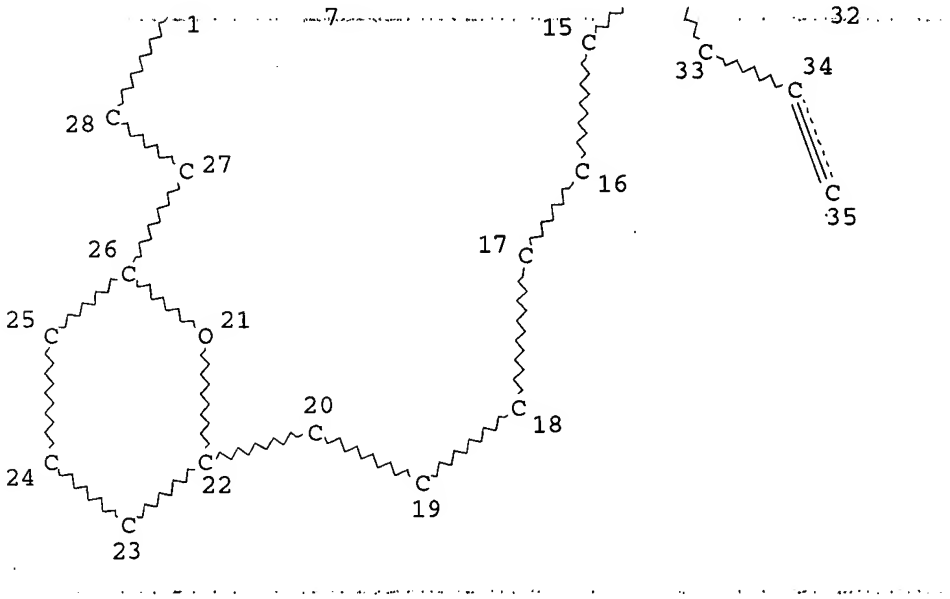

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NSPEC IS R AT 3
NSPEC IS R AT 4

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  47

STEREO ATTRIBUTES: NONE
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L22           16 SEA FILE=MARPAT SSS FUL L3
L23           13 SEA FILE=MARPAT ABB=ON  PLU=ON  L22 NOT L18
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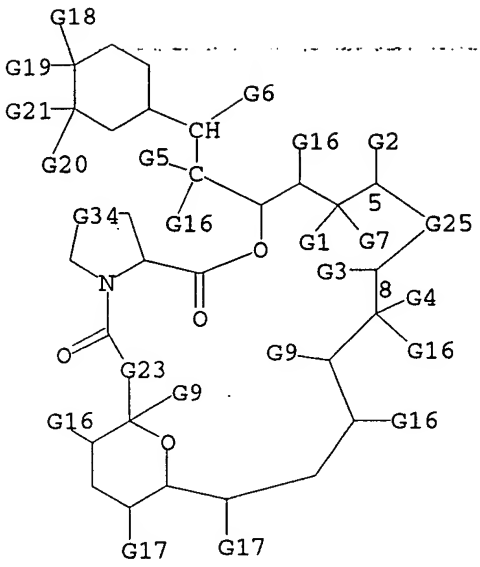
=> d 123 ibib abs qhit 1-13

L23 ANSWER 1 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:207222 MARPAT
TITLE: Pharmaceutical compositions containing tricyclic compounds
INVENTOR(S): Yamanaka, Masayuki; Shimojo, Fumio; Ueda, Satoshi; Toyoda, Toshihiko; Ibuki, Rinta; Ohnishi, Norio
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836747	A1	19980827	WO 1998-JP665	19980218
W: AU, BR, CA, CN, HU, IL, JP, KR, MX, NO, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
TW 450810	B	20010821	TW 1998-87102169	19980217
CA 2282345	AA	19980827	CA 1998-2282345	19980218
AU 9862289	A1	19980909	AU 1998-62289	19980218
AU 727337	B2	20001207		
EP 977565	A1	20000209	EP 1998-904366	19980218
EP 977565	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9807234	A	20000425	BR 1998-7234	19980218
JP 2000513739	T2	20001017	JP 1998-536482	19980218
JP 3396888	B2	20030414		
AT 237325	E	20030515	AT 1998-904366	19980218
ES 2193515	T3	20031101	ES 1998-904366	19980218
PT 977565	T	20040130	PT 1998-904366	19980218
IL 131298	A1	20040620	IL 1998-131298	19980218
ZA 9801391	A	19980824	ZA 1998-1391	19980219
MX 9907451	A	20000228	MX 1999-7451	19990812
NO 9904003	A	19991019	NO 1999-4003	19990819
US 2002032212	A1	20020314	US 1999-367698	19990820
US 6387918	B2	20020514		
PRIORITY APPLN. INFO.:			JP 1997-36172	19970220
			JP 1997-256357	19970922
			WO 1998-JP665	19980218

AB A pharmaceutical composition comprising a tricyclic compound or its pharmaceutically acceptable salt, an oil substance, a surfactant, a hydrophilic substance, water, and optionally a pH control agent, with enhanced stability, absorbability and/or a low irritation potential, is provided. A cream contained FK506 0.1, iso-Pr myristate 25.0, polyoxyethylene cetyl ether 5.0, water 68.9, and Carbopol940 1.0%. The area under the blood concentration-time curve over 0-24 hors after transdermal application to the mice was >30 ng.h.mL.

MSTR 1



G7 = 56

56 O—G8

G8 = 138

138 C(O)N(G32)—G32

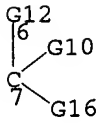
G9 = OH
G10 = CH2CH=CH2
G12 = C(O)
G16 = alkyl / Me
G17 = OMe
G19 = 82

82 O—G8

G21 = 88

88 O—CH2—O—CH2—CH2—OMe

G23 = C(O)
G25 = 6-5 7-8



G34 = (1-2) CH2
DER: or pharmaceutically acceptable salts
MPL: claim 1

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

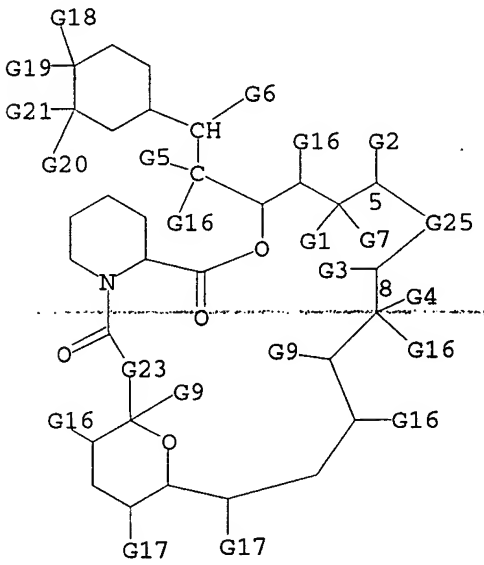
L23 ANSWER 2 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:297667 MARPAT
TITLE: Aerosol compositions containing triglycerides and tricyclic compounds
INVENTOR(S): Murata, Saburo; Shimojo, Fumio; Tokunaga, Yuji; Hata, Takehisa
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9710806	A1	19970327	WO 1996-JP2670	19960918
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2232378	AA	19970327	CA 1996-2232378	19960918
ZA 9607887	A	19970407	ZA 1996-7887	19960918
AU 9669998	A1	19970409	AU 1996-69998	19960918
AU 719613	B2	20000511		
JP 09143054	A2	19970603	JP 1996-246053	19960918
JP 3266005	B2	20020318		
EP 851753	A1	19980708	EP 1996-931227	19960918
EP 851753	B1	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1201384	A	19981209	CN 1996-198166	19960918
JP 2000505050	T2	20000425	JP 1997-512589	19960918
JP 3362394	B2	20030107		
AT 254450	E	20031215	AT 1996-931227	19960918
PT 851753	T	20040430	PT 1996-931227	19960918
ES 2206590	T3	20040516	ES 1996-931227	19960918
TW 429153	B	20010411	TW 1996-85111460	19960919
US 6361760	B1	20020326	US 1998-29863	19980422
HK 1017845	A1	20041210	HK 1999-102062	19990507
US 2002061906	A1	20020523	US 2001-994702	20011128
US 6524556	B2	20030225		
PRIORITY APPLN. INFO.:			JP 1995-239342	19950919
			WO 1996-JP2670	19960918
			US 1998-29863	19980422

AB The use of a medium-chain fatty acid triglyceride as the dispersant in the preparation of a medicinal aerosol composition comprising a tricyclic compound such as

FK 506 dispersed in a liquefied hydrofluoroalkane propellant is described. When a liquefied hydrofluoroalkane is added to a kneaded premix of the tricyclic compound and a medium-chain fatty acid triglyceride, the active ingredient is evenly dispersed in the liquefied hydrofluoroalkane. Therefore, by distributing a dispenser first with the kneaded premix and, then, with a liquefied hydrofluoroalkane under cooling or elevated pressure, an aerosol composition is obtained having an improved uniformity of content of the active ingredient. Thus, an aerosol was prepared containing FK 506 506 10 mg, Miglyol 812 25 mg, and HFA-27 5 mL.

MSTR 1B



G7 = 56

56 O—G8

G8 = 138

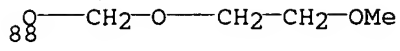
G32

138 C(O)N—G32

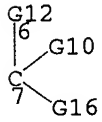
G9 = OH
G10 = CH2CH=CH2
G12 = C(O)
G16 = alkyl / Me
G17 = OMe
G19 = 82

82 O—G8

G21 = 88



G23 = C(O)
G25 = 6-5 7-8



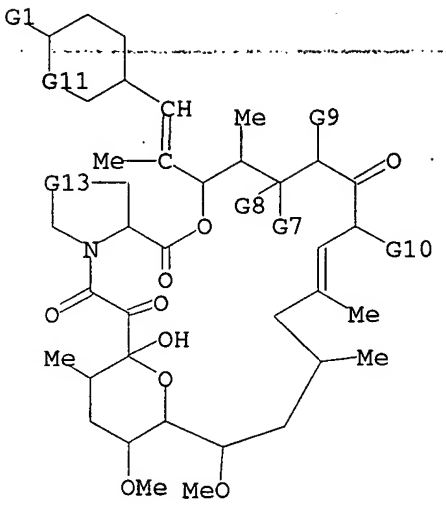
DER: or pharmaceutically acceptable salts
MPL: claim 1

L23 ANSWER 3 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:350482 MARPAT
TITLE: Method for assaying calcineurin-inhibiting immunosuppressants
INVENTOR(S): Kobayashi, Masakazu; Tamura, Kouichi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9524645	A1	19950914	WO 1995-JP372	19950308
W: AU, CA, CN, JP, KR, MX, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2185105	AA	19950914	CA 1995-2185105	19950308
AU 9518617	A1	19950925	AU 1995-18617	19950308
AU 686762	B2	19980212		
EP 750193	A1	19961227	EP 1995-910762	19950308
EP 750193	B1	20021127		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1147853	A	19970416	CN 1995-192949	19950308
AT 228657	E	20021215	AT 1995-910762	19950308
JP 3551431	B2	20040804	JP 1995-523355	19950308
US 6338946	B1	20020115	US 1999-457395	19991209
PRIORITY APPLN. INFO.:			JP 1994-39534	19940310
			WO 1995-JP372	19950308
			US 1996-702549	19961024

AB This invention relates to a method and kit for assaying calcineurin-inhibiting immunosuppressants (e.g. FK506 and cyclosporin A) by determining a complex containing immunophilin, calcineurin, calmodulin, calcium ions and test immunosuppressant. Using the above method and kit, it is possible to determine more accurately the total concentration of the substances actually having the immunosuppressant effect in the determination of the blood level of calcineurin-inhibiting immunosuppressants.

MSTR 1



G1 = 51

51 O—G2

G2 = CONH2 (SO)
G7 = 59

59 O—G2

G10 = CH2CH=CH2
G11 = 64

64 HC—G12

G12 = OMe
G13 = (1-2) CH2
MPL: claim 3
NTE: substitution is restricted

L23 ANSWER 4 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:55593 MARPAT
TITLE: FR 520 derivatives as immunosuppressants
INVENTOR(S): Baumann, Karl
PATENT ASSIGNEE(S): Sandoz-Patent-GmbH, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

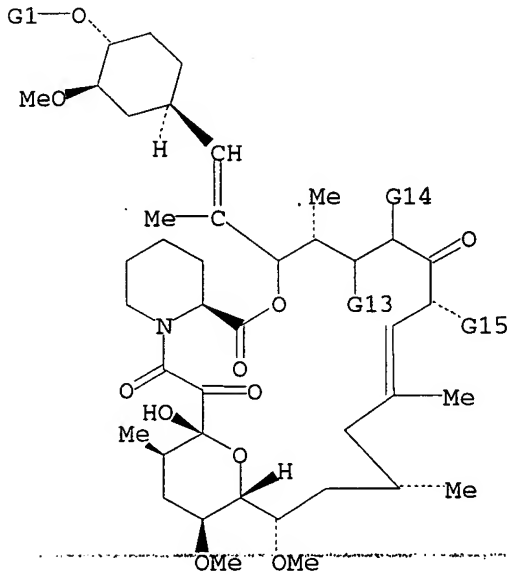
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4336458	A1	19950427	DE 1993-4336458	19931026

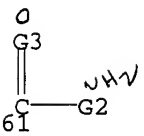
PRIORITY APPLN. INFO.: DE 1993-4336458 19931026

AB FR 520 derivs. substituted in the 33-position by carbamoyl, thiocarbamoyl, carbonate, or thiocarbonate groups were prepared for use as immunosuppressants (no data). Thus, 24-O-tert-butyldimethylsilyl-FR 520 was treated with ClCO2CCl3 to give the 33-carbamoyl derivative which was desilylated with HF.

MSTR 1

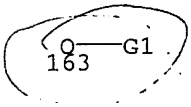


G1 = 61



2-carbamoyl

G2 = NH2
G3 = O
G13 = 163



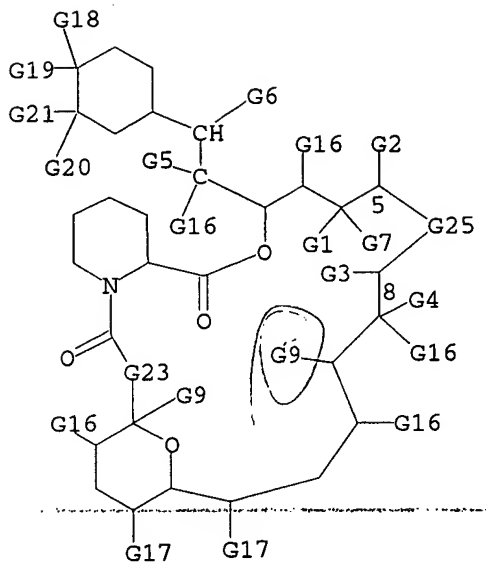
G15 = CH2CH=CH2
MPL: claim 1

L23 ANSWER 5 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 122:115005 MARPAT
TITLE: Anti-proliferative lotions containing tricyclic compounds
INVENTOR(S): Kagayama, Akira; Tanimoto, Sachiyo; Murata, Saburo; Hata, Takehisa
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9428894	A1	19941222	WO 1994-JP863	19940530
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 06345646	A2	19941220	JP 1993-137924	19930608
CA 2164838	AA	19941222	CA 1994-2164838	19940530
AU 9468162	A1	19950103	AU 1994-68162	19940530
AU 684286	B2	19971211		
CN 1124925	A	19960619	CN 1994-192387	19940530
CN 1100538	B	20030205		
EP 753297	A1	19970115	EP 1994-916418	19940530
EP 753297	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 224710	E	20021015	AT 1994-916418	19940530
ES 2179074	T3	20030116	ES 1994-916418	19940530
PT 753297	T	20030228	PT 1994-916418	19940530
US 5939427	A	19990817	US 1998-2887	19980105
PRIORITY APPLN. INFO.:			JP 1993-137924	19930608
			WO 1994-JP863	19940530

AB A lotion comprises a tricyclic compound represented by 17-allyl-1,14-dihydroxy-12-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylvinyl]-23-25,-dimethoxy-13,19,21,27-trimethyl-11,28-dioxa-4-azatricylo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetrone or a pharmaceutically acceptable salt thereof, a dissoln./absorption promoter, a liquid medium, and optionally an emulsifying agent or a mixture thereof with a thickening agent. The lotion is stable and excellent in absorbability, scarcely irritates the skin, and can be sustainedly released. It is useful for treating and preventing inflammatory and proliferative dermatoses and immunol. mediated skin diseases. For example, a lotion containing FK 506 100 mg, iso-Pr myristate 1 mL, and ethanol 4 mL was formulated.

MSTR 1B



G7 = 56

56 O—G8

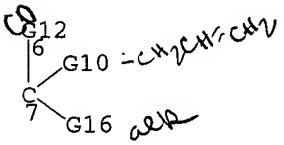
G8 = alkylaminocarbonyl<(1-6)> (SR CO2H (SO))
G9 = OH
G10 = CH2CH=CH2
G12 = C(O)
G16 = alkyl / Me
G17 = OMe
G19 = 82

82 O—G8

G21 = 88

88 O—CH2—O—CH2—CH2—OMe

G23 = C(O)
G25 = 6-5 7-8



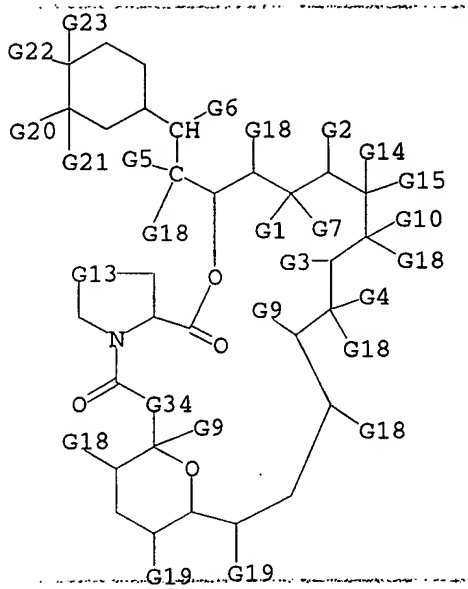
DER: or pharmaceutically acceptable salts
MPL: claim 1

L23 ANSWER 6 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 119:34331 MARPAT
TITLE: Liposome preparation containing immunosuppressant tricyclic compound
INVENTOR(S): Kagayama, Akira; Tokunaga, Yuji; Kaibara, Atsunori; Tanimoto, Sachiyo; Hata, Takehisa
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

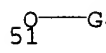
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9308802	A1	19930513	WO 1992-JP1388	19921026
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
EP 658344	A1	19950621	EP 1992-921787	19921026
EP 658344	B1	20000105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
AT 188378	E	20000115	AT 1992-921787	19921026
ES 2140419	T3	20000301	ES 1992-921787	19921026
CA 2122344	C	20040420	CA 1992-2122344	19921026
US 5817333	A	19981006	US 1995-446305	19950522
GR 3032319	T3	20000427	GR 1999-403375	20000107
PRIORITY APPLN. INFO.:			JP 1991-313422	19911031
			WO 1992-JP1388	19921026
			US 1994-211834	19940429

AB A liposome formulation contains a tricyclic compound such as 17-allyl-1,14-dihydroxy- 12-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylvinyl]-23,25-dimethoxy-13,1921,27-tetramethyl-11,28-dioxa-4-azatricyclo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetraone (FK 506) and its analog, encapsulated by liposomal membrane. Egg yolk phosphatidylcholine, cholesterol, phosphatidylserine, FK 506 were dissolved in a CHCl3/MeOH mixture, dried under reduced pressure to form thin membranes, treated with a phosphate buffer to give a liposome suspension, and finally filtered to isolate liposome particles containing FK 506.

MSTR 1A



G7 = 51



G8 = loweralkylaminocarbonyl (SO (1-) G27)
G9 = OH
G10 = CH2CH=CH2
G13 = (1-3) CH2
G14 = OH
G18 = alkyl / Me
G19 = OMe
G20 = acyloxy
G22 = 93

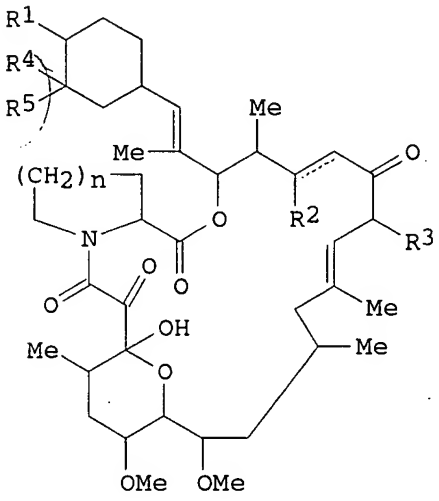
G34 = C(O)
DER: or pharmaceutically acceptable salts
MPL: claim 1

L23 ANSWER 7 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 117:124480 MARPAT
TITLE: Enhancers for antitumor activity of azatricyclooctacosaene derivatives
INVENTOR(S): Tsuruo, Takashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03240726	A2	19911028	JP 1990-34571	19900215
PRIORITY APPLN. INFO.:			JP 1990-34571	19900215

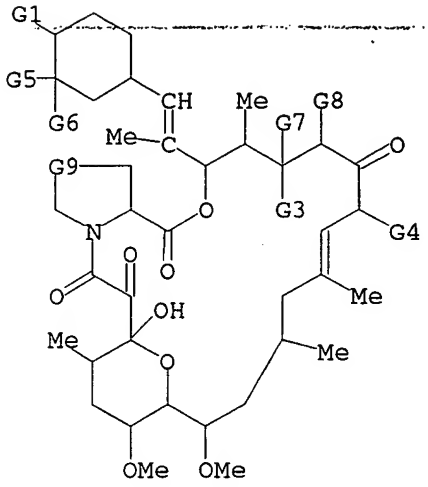
GI



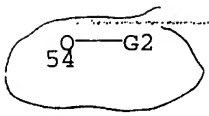
I

AB The title neoplasm inhibitor enhancers contain compds. I [R1 = (protected) OH; R2 = H, (protected) OH; R3 = Me, Et, Pro, allyl; R4 = OH, OMe; R5 = H, oxo (with R4); n = 1, 2 integer; the symbol shown by a solid line and a broken line (SL) means a single bond or a double bond; R2 ≠ protected OH when R4 = OH and R5 = H, or R4 and R5 = oxo] or their pharmaceutically acceptable salts. I are known immunosuppressants and increase the intracellular I concns. in chemotherapy. FK506 (I: R1 = OH, R2 = OH, R3 = allyl, R4 = OMe, R5 = H, n = 2, SL = single bond) enhanced the leukemia cell-inhibiting activity of vincristine as reflected by the 50% inhibition concns. FK506 at 100 mg/kg i.p. caused no mortality in mice. FK506 (1 g) was dissolved in 10 mL EtOH, mixed with 1 g hydroxypropyl Me cellulose 2910 (TC-5T), 5 mL CH2Cl2, 2 g lactose, and 1 g AcDiSol, dried, and pulverized to give 5 g solid solution composition

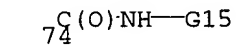
MSTR 1



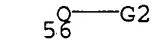
G1 = 54



G2 = 74



G3 = 56

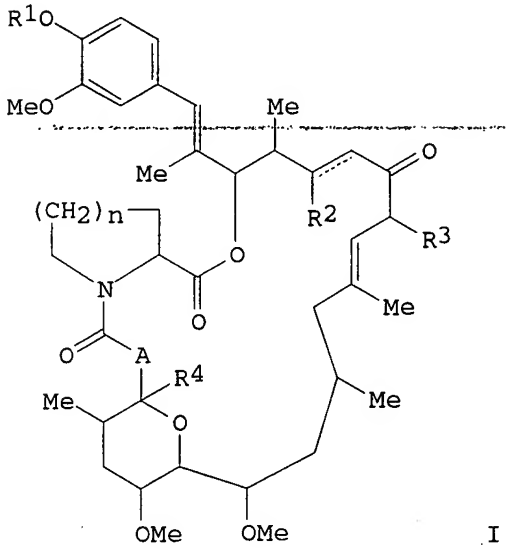


G4 = CH2CH=CH2
G5 = OMe
G9 = (1-2) CH2
DER: or pharmacologically acceptable salts
MPL: claim 1
NTE: substitution is restricted

L23 ANSWER 8 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:235667 MARPAT
TITLE: Preparation of dioxaazatricyclooctacosenetetraone
INVENTOR(S): Kasahara, Chiyoshi; Ohkawa, Takehiko; Hashimoto, Masashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Brit. UK Pat. Appl., 26 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2244991	A1	19911218	GB 1990-12963	19900611
PRIORITY APPLN. INFO.:			GB 1990-12963	19900611

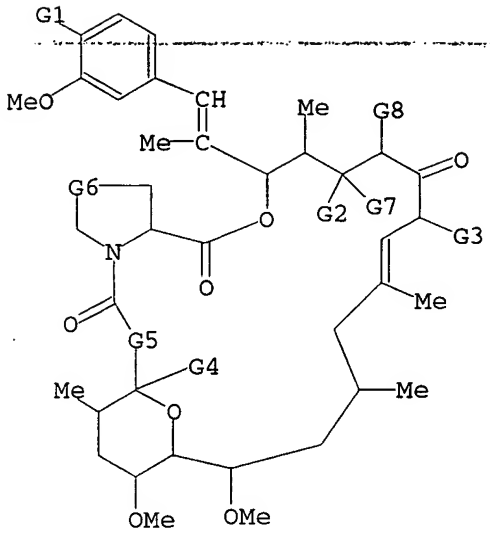
GI



I

AB Title compds. I (R1 = H, acyl; R2 = H, HO, acyloxy; R3 = Me, Et, Pr, allyl; R4 = HO, alkoxy; A = CH2, CO; n = 1, 2; dotted line = optional double bond) and salts thereof, useful for treating or preventing resistance to transplantation, graft-vs-host diseases by medulla ossium, autoimmune diseases and infectious diseases (no data), are prepared To a solution of 1-hydroxy-12-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylvinyl]-23,25-dimethoxy-13,19,21,27-tetramethyl-11,28-dioxa-17-propyl-4-azatricyclo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetraone in C6H6 were added ethylene glycol and p-MeC6H4SO3H successively, the mixture refluxed azeotropically for 8 h to give the appropriate 16-ethylene acetal, which was then oxidized, dehydrogenated twice, and deacetalated to give I (R1 = R2 = H, R3 = Pr, R4 = HO, A = CO, n = 2, no addnl. double bond).

MSTR 1



G1 = 54

54 O—G10

G2 = 56

56 O—G10

G3 = CH2CH=CH2
G4 = OH
G5 = C(O)
G6 = (1-2) CH2
G10 = 73

73 C(O)-NH—G18

DER: and salts
MPL: claim 1

L23 ANSWER 9 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:173897 MARPAT
TITLE: Preparation of tricyclic compounds as immunosuppressants and antimicrobials
INVENTOR(S): Kasahara, Chiyoshi; Ohkawa, Takehiko; Hashimoto, Masashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

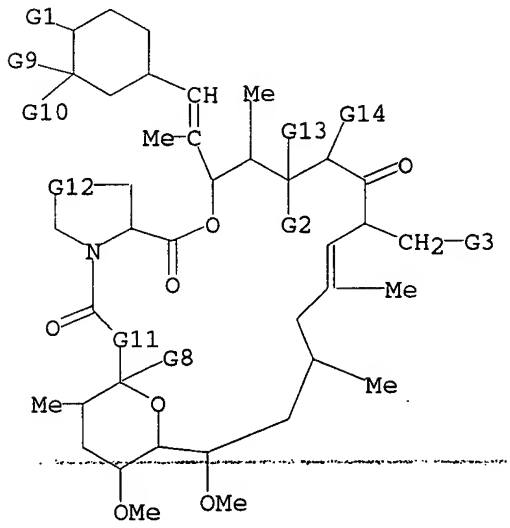
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200313	A1	19920109	WO 1991-JP811	19910618
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
EP 536401	A1	19930414	EP 1991-911075	19910618
R: CH, DE, FR, GB, IT, LI				
JP 06501920	T2	19940303	JP 1991-510112	19910618
PRIORITY APPLN. INFO.:			GB 1990-14136	19900625
			WO 1991-JP811	19910618

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Tricyclic compds. [I; R1 = H, acyl; R2 = H, OH, alkoxy, acyloxy; R3 = C3-7 alkyl, aralkyl, alkenyl, etc.; R4 = OH, alkoxy; R5 = H, R6 = OH, MeO; R5R6 = oxo; A = CH2, CO, CH(OH); n = 1, 2; dotted line = optional double bond] are prepared Hydroxylation of 2.57 g allyl compound II (R = vinyl) with OsO4 gave 1.91 g dihydroxypropyl derivative II [R = HOCH2CH(OH)], which (220 mg) was oxidized with NaIO4 to give 220 mg aldehyde II (R = CHO) (III). Wittig reaction of 150 mg III with BuP+Ph3 Br- in Et2O gave 38 mg hexenyl derivative II (R = CH:CHPr), which (32 mg) was hydrogenated over Rh-Al2O3 to give 25 mg hexyl derivative II (R = pentyl). I (R1 = Me, R2 = R4 = R5 = OH, R3 = 1-propenyl, R6 = H, A = CO, n = 2, dotted line = single bond) showed IC50 of 4.1 + 10-9M in suppression of in vitro mixed lymphocyte reaction.

MSTR 1



G1 = 69

69 O—C(O)-NH—G15

G2 = 90

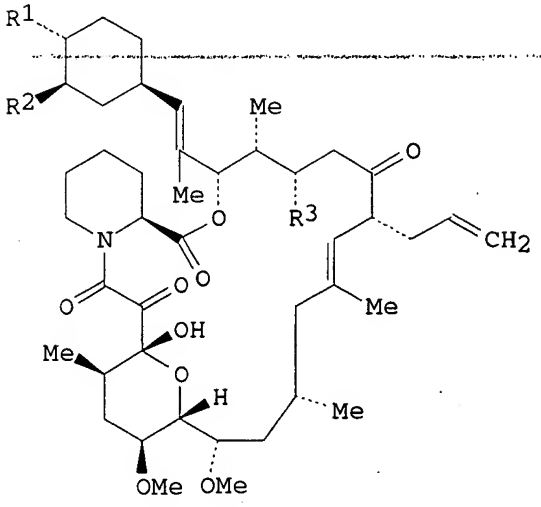
90 O—C(O)-NH—G15

G3 = alkenyl<(3-7)>
G8 = OH
G10 = OMe
G11 = CHOH
G12 = (1-2) CH2
DER: or pharmaceutically acceptable salts
MPL: claim 1

L23 ANSWER 10 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:104486 MARPAT
TITLE: TAN-1313, its acyl derivatives, and water-soluble preparations containing them
INVENTOR(S): Tanida, Seiichi; Harada, Setsuo
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03178978	A2	19910802	JP 1990-262665	19900928
JP 3054741	B2	20000619		
PRIORITY APPLN. INFO.:			JP 1989-256191	19890929

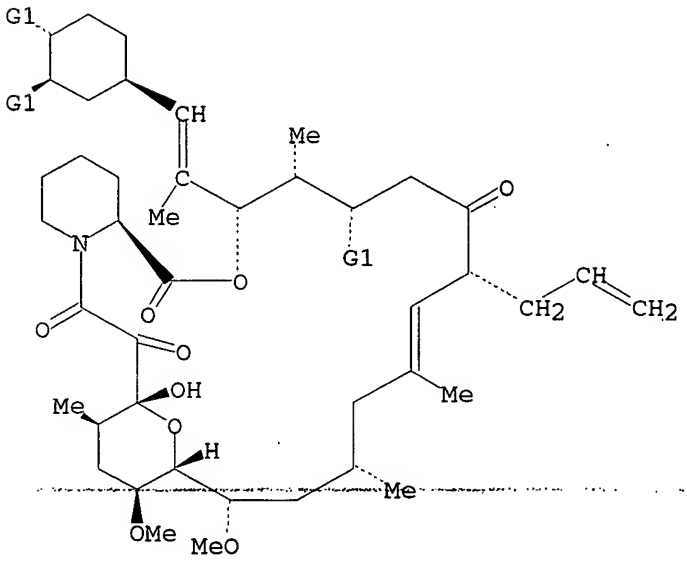
GI



I

AB TAN-1313 (I; R1-3 = OH) (II) and its triacyl derivs. I (R1-3 = acyloxy), useful as immunosuppressants, are manufactured from FK506. II is manufactured from FK506 with culture media of Streptomyces or Amycolatopsis or their prepns. I (R1, R2, R3 = H, OH, OR; R = organic residue) is solubilized in water using cyclic polysaccharides. S. tolypophorus IFO 1315 was precultured in a medium containing glucose, tryptone, and yeast extract at 28° for 48 h, cultured in the same medium at 28° for 24 h, mixed with MeOH solution of FK506, and further cultured for 24 h to produce 220 mg II from 20 L medium. Crude II (.apprx.80 mg) in pyridine was treated with Ac2O at room temperature for 7 h to give 25 mg II triacetyl derivative

MSTR 2



G1 = 59

59 O—G2

G2 = aralkyl (SO (1-) G6) / 61

61 C(O)-G3

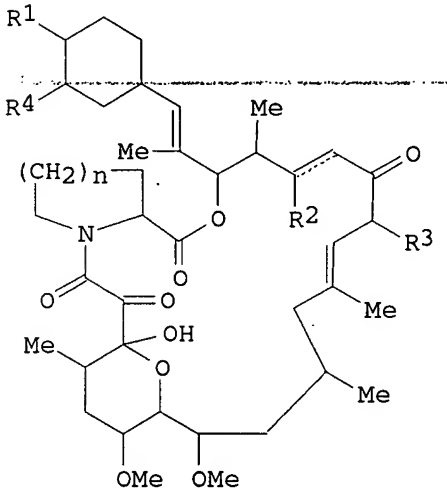
G3 = NH2
MPL: claim 3

L23 ANSWER 11 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:76365 MARPAT
TITLE: Methods for treating and preventing inflammation of mucosa and blood vessels using FK 506 and related

compounds
INVENTOR(S): Kubes, Paul; Hunter, James; Granger, D. Neil
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117754	A1	19911128	WO 1991-US3185	19910513

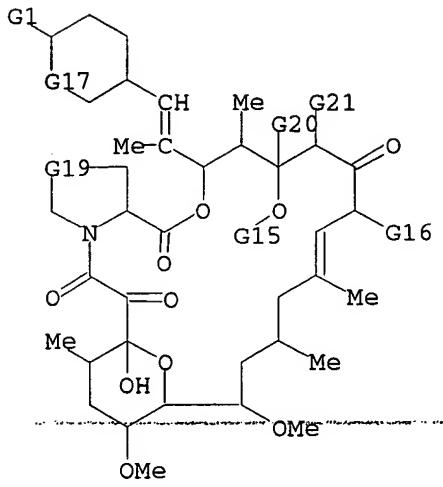
W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
PRIORITY APPLN. INFO.: US 1990-522145 19900511
GI



I

AB Macrolides I [R1 = (protected) OH; R2 = H, (protected) OH; R3 = Me, Et, Pr, allyl; R4 = HO, MeO, :O; n = 1, 2] and their salts, such as FK 506, are useful for treating or preventing the title diseases, e.g. LTB4-mediated diseases, gastric ulcers, vascular damage from ischemic diseases and thrombosis, ischemic bowel disease, inflammatory bowel disease, necrotizing enterocolitis, and burn-associated intestinal lesions. Thus, cats with exptl. intestinal ischemia showed mucosal infiltration by neutrophils (determined from mucosal myeloperoxidase activity) which was lessened by treatment with FK 506 (0.3 mg/kg/day i.m. Capsules were prepared by dissolving 1 g FK 506 in 10 mL EtOH, adding 1 g hydroxypropylmethylcellulose 2910 to form a suspension, dissolving in 5 mL CH2Cl2, adding 2 g lactose and 1 g croscarmellose Na, evaporating off the solvent, and grinding, sieving, and encapsulating the dry product.

MSTR 1D



G1 = 62

62 O—G2

G2 = 72

72 C(O)-G5

G5 = loweralkylamino (SR (1-) CO2H)
G15 = 126

126 C(O)—G22

G16 = CH2CH=CH2
G17 = 120

120 HC—G18

G18 = OMe
G19 = CH2CH2
G22 = loweralkylamino (SR (1-) CO2H)
MPL: claim 1

L23 ANSWER 12 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 115:279490 MARPAT
TITLE: Preparation of (dimethoxycyclohexyl)oxopentamethylnona decadi(tri)enoate derivatives and their lactones as immunosuppressives
INVENTOR(S): Cooper, Martin Edward; Donald, David Keith; Tanaka, Hirokazu

PATENT ASSIGNEE(S): Fisons PLC, UK; Fujisawa Pharmaceutical Co., Ltd.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

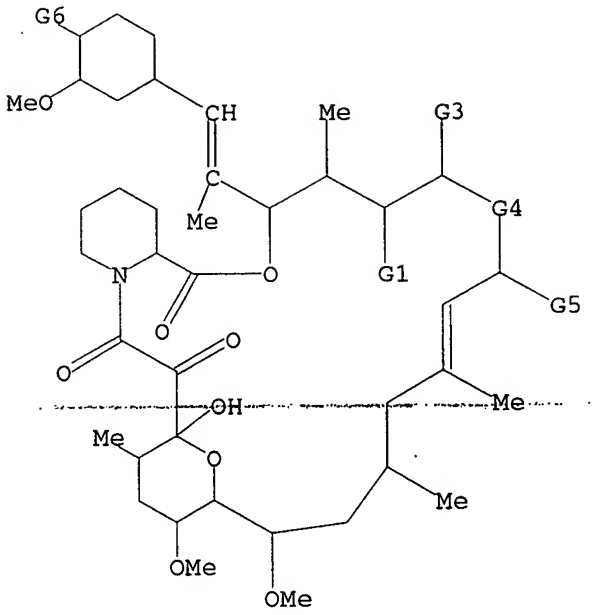
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 444829	A2	19910904	EP 1991-301431	19910222
EP 444829	A3	19920603		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 04217939	A2	19920807	JP 1991-53588	19910227
US 5210227	A	19930511	US 1991-661802	19910227
PRIORITY APPLN. INFO.:			GB 1990-4396	19900227
			GB 1990-9485	19900427

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, (protected) OH, alkoxy; R2 = H; R3 = O or H, OH; R4 = Me, Et, Pr, CH2CH:CH2; R5 = (protected) OH, alkoxy; R6 = OH; R7 = OH, alkoxy, NR8R9; R8, R9 = H, alkyl, aryl; R6 and R7 together may equal O; R1R2 may equal a double bond; with provisos] were prepared as immunosuppressives. Thus MeNH2.HCl was dissolved in MeOH and a solution of NaOH in MeOH was added. The resulting solution was added to macrolide II R1, R5 = OH; R2 = H; R3, R10 = O; R4 = allyl), followed by a solution of NaCNBH3 in MeOH. Thus solution was stirred for 1.5 h at 20° to give title compound I (R1, R5 = OH, R2 = H, R3 = O, R4 = allyl, R6 = Me, R7 = OMe). A similar I (R1 = H, R4 = Pr, all others as above) had IC50 of 1 + 10-7M against a mixed lymphocyte reaction.

MSTR 2



G1 = 19

19 O—G2

G2 = 82

82 C(O)NH—G18

G4 = C(O)
G5 = CH2CH=CH2
G6 = 42

42 O—G2

DER: and pharmaceutically acceptable salts
MPL: claim 8
NTE: substitution is restricted

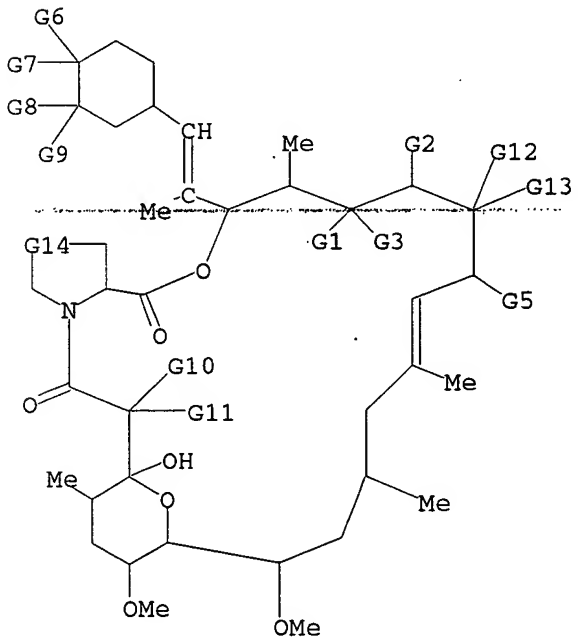
L23 ANSWER 13 OF 13 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 115:99270 MARPAT
TITLE: Pharmaceutical compns. containing macrolide antibiotics for the treatment of reversible obstructive airways diseases
INVENTOR(S): Norris, Alan Anthony; Jackson, Dale Michael; Makino, Sohei; Fukuda, Takeshi; Akutsu, Ikuo
PATENT ASSIGNEE(S): Fisons PLC, UK; Fujisawa Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

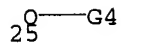
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9014826	A1	19901213	WO 1990-GB866	19900606
W: AU, CA, FI, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
JP 03291225	A2	19911220	JP 1990-96045	19900409
CA 2054203	AA	19901207	CA 1990-2054203	19900606
CA 2054203	C	20010821		
AU 9057214	A1	19910107	AU 1990-57214	19900606
AU 639460	B2	19930729		
EP 475994	A1	19920325	EP 1990-908603	19900606
EP 475994	B1	19940914		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05503283	T2	19930603	JP 1990-508050	19900606
JP 2508918	B2	19960619		
ES 2061043	T3	19941201	ES 1990-908603	19900606
US 5519049	A	19960521	US 1993-93305	19930716
PRIORITY APPLN. INFO.:			GB 1989-12935	19890606
			JP 1990-96045	19900409
			WO 1990-GB866	19900606
			US 1992-781190	19920127

AB Pharmaceuticals containing 17-allyl-1,14-dihydroxy-12-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylvinyl]-23,25-dimethoxy-13,19,21,27-tetramethyl-11,28-dioxa-4-azatricyclo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetraone and its derivs. (Markush structure given) are prepared for the treatment of reversible obstructive airways disease, particularly asthma.

MSTR 1

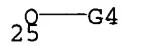


G3 = 25

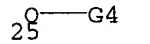


G4 = 76

G5 = CH2CH=CH2
G7 = 25



G9 = 25



G11 = OH
G13 = OH
G14 = (1-2) CH2
G15 = CH2
G20 = NH
DER: or pharmaceutically acceptable derivatives
MPL: claim 1